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A DISSERTATION SUBMITTED TO THE FACULTY OF THE DIVISION OF THE BIOLOGICAL SCIENCES IN CANDIDACY FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF PHYSIOLOGY
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INCREASED COLLATERAL BLOOD SUPPLY TO THE KIDNEY IN RENAL HYPERTENSION*†

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THE production of persistent hypertension by chronic renal ischemia[1] suggested to us, as it has to several other workers,[2-5] that an increase in the collateral blood supply to the ischemic kidney might relieve the ischemia and possibly the hypertension. This thesis was tested in eighteen dogs. The efficacy of the collateral supply was judged by the effect upon the course of the hypertension and by the anatomical evidence of cortical vascularity.

Blood pressures were obtained with the Hamilton needle manometer[6] on trained, unanesthetized dogs, according to the method previously described by us.[7] All the operations were carried out under nembutal anesthesia with aseptic technique. The kidneys were decapsulated and brought into close contact with the denuded posterior and lateral muscle walls (myopexy) in order to facilitate the development of a collateral blood supply either before or after the development of the hypertension. The Goldblatt technique[1] was used to produce the hypertension.

At the termination of each experiment, the dog was anesthetized with nembutal, the renal arteries ligated, and India ink injected into the thoracic aorta. The animal was sacrificed within a few minutes. The kidneys were then examined to determine the extent of the collateral blood supply, as indicated by the amount of the India ink which had entered the kidney.

Group 1.—(a) In two normotensive dogs simple unilateral decapsulation was performed. A month later India-ink injection showed no demonstrable difference in the amount of ink in the operated and unoperated kidneys. (b) In two normotensive dogs the omentum was brought in contact with a decapsulated kidney. A month later India-ink injection showed a slightly greater amount of India ink in the operated kidneys than in the unoperated ones. (c) Unilateral decapsulation with the production of a muscle bed was performed in four normotensive dogs. A month later the India-ink injection showed approximately twice as much India ink in the decapsulated kidney as in the unoperated kidney. At autopsy it was observed that an adherent scar tissue capsule completely surrounded each of the decapsulated kidneys.

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Group 2.—In three dogs with hypertension of 169, 79, and 39 days' duration, decapsulation and the production of a muscle bed for the ischemic kidneys caused only a transient fall in blood pressure. Fig. 1 shows the protocol of the last animal. However, the blood pressures returned to the hypertensive levels within three to twenty days, and these elevated pressures were maintained until the dogs were sacrificed 267, 81, and 96 days later, respectively. In one of these animals the main renal arteries were tied off completely 220 days after the muscle-bed operation. Unlike the effect in kidneys without a muscle bed, renal excretory insufficiency did not develop; however, the blood pressure mounted to higher levels and the animal was sacrificed 47 days later. As in the normotensive dogs of Group 1, India-ink injection in these three animals showed the development of an extensive collateral circulation, and adherent scar tissue capsules completely surrounded the decapsulated kidneys.

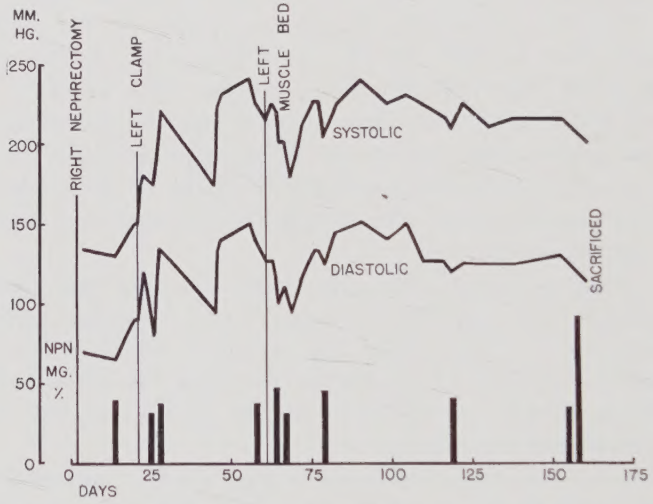

Fig. 1.—(Dog U-84.) The effect of decapsulation and myopexy on a pre-existing renal hypertension. The right kidney had been removed some days previous to the application of a Goldblatt clamp to the left renal artery. Hypertension followed the latter operation. The production of a muscle bed after decapsulating this kidney 41 days later had only a transient depressor effect. Hypertension then persisted for 96 days until the animal was sacrificed. Note the late development of an elevation of the blood N.P.N. At necropsy, the India-ink injection made ante mortem demonstrated the presence of a good collateral blood supply through the cortex from the perirenal adhesions. An extensive thick scar encompassed the kidney. In the figure the blood pressure is shown by curves, the systolic above and the diastolic below. The blood N.P.N. values are given by the height of the vertical blocks, and the time at which various procedures were carried out are shown by vertical lines. Zero time is taken as the time when the animal had been properly trained.

Group 3.—The prophylactic effect of the production of a collateral blood supply previous to the renal arterial clamping was studied in six dogs. In five, decapsulation and the production of a muscle bed were performed about one month before the establishment of renal ischemia. The protocol of one of these animals is shown in Fig. 2. In a uninephrectomized dog the muscle bed and the Goldblatt clamp were simultaneously applied to the remaining kidney (Fig. 3). Hyperten-

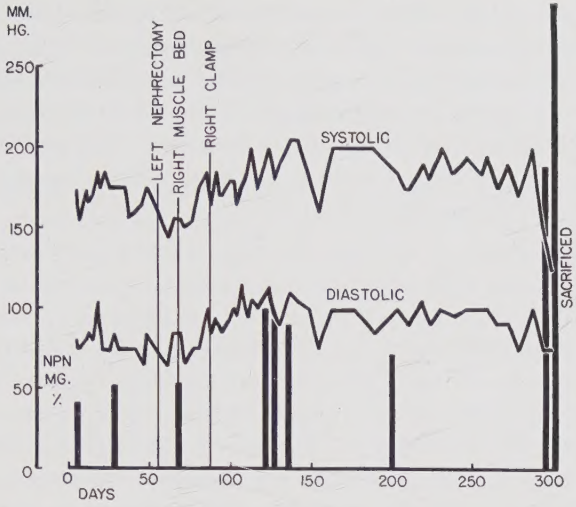

Fig. 2.—(Dog U-21.) The effect of decapsulation and myopexy on the action of subsequent constriction of its renal artery. The left kidney had been removed at an earlier operation. Twenty-one days after decapsulation and the application of a muscle bed to the right kidney, a Goldblatt clamp was applied to the renal artery. Hypertension as well as renal excretory insufficiency developed following this last procedure; these persisted with a terminal increase in the latter, leading to a marked uremia 211 days later, at which time the animal was sacrificed. At necropsy, the India-ink injection made ante mortem revealed a good collateral blood supply through the cortex from the perirenal adhesions. An extensive scar encompassed the kidney. Conventions are the same as in Fig. 1.

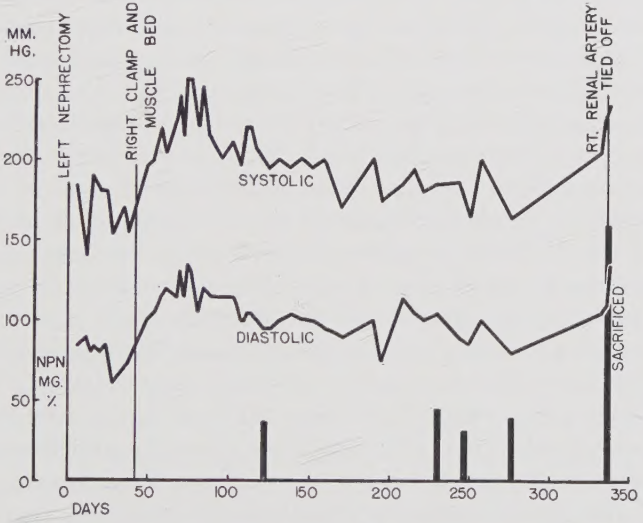

Fig. 3.—(Dog K-7.) The effect of a decapsulation and myopexy simultaneously with a partial constriction of its renal artery. The left kidney had been removed in an earlier operation. The combined operations on the right kidney resulted in hypertension, which was most marked soon after the operation, as is often the case in animals even when no myopexy and decapsulation are done. The right renal artery was completely tied off 293 days after the operation, and it was found that the collateral blood supply was not sufficient to prevent a further elevation of pressure and the development of uremia. The animal was sacrificed 3 days after the complete renal artery ligation. At necropsy, the India-ink injection made ante mortem demonstrated the presence of a good collateral blood supply through the cortex from the perirenal adhesions. An extensive thick scar encompassed the kidney. Conventions are the same as in Fig. 1.

sion developed in all except one of these animals, which is similar to our experience in producing hypertension without a muscle bed. In one other dog decapsulation and myopexy appeared to lead to hypertension, even without the application of the Goldblatt clamp. In this series India-ink injection showed the presence of numerous functioning capsular-cortical blood vessels, but scar tissue capsules completely surrounded the decapsulated kidneys.

The natural tendency for the blood pressure to return to normal in hypertensive dogs with renal ischemia without special procedures to bring this about has been observed in our laboratory[7] and has been the subject of reports by other investigators.[8] This disappearance or partial alleviation of the hypertension has been associated with the development of large collateral blood vessels entering the capsule and pelvis of the ischemic kidney. The newly developed accessory circulation may be sufficient to permit the kidney to carry on its function even after progressive and complete obliteration of the main renal arteries.

In view of the large accessory blood supply which is developed without aid by an ischemic kidney, decapsulation and myopexy might be expected to result in an even greater collateral supply and thereby facilitate the relief of the ischemia and possibly the hypertension. The statement of Goldblatt[9] that renal decapsulation with myo- or omentopexy may interfere with the pronounced elevation of the blood pressure in experimental renal ischemia might be so interpreted. Our results show definitely that this is not the case. Although a demonstrable accessory supply through the cortex does develop and may neutralize the tendency toward renal excretory insufficiency, the formation of a scar-tissue capsule to take the place of the natural capsule which has been stripped off appears to prevent the development of sufficient adventitious blood vessels to relieve the ischemia. The tendency of this fibrous capsule to shrink, its relative lack of distensibility when compared to the natural capsule, and its close adherence to the cortex of the kidney all serve to place the decapsulated kidney at a disadvantage.[10] Further, envelopment of the kidney in a relatively inflexible capsule interfering with the normal fluctuations in kidney volume which occur during the cardiac cycle may lead to anuria[11] or even to hypertension.[12] Slight increases in the intrarenal pressure, which might be brought about by the rigid capsule, also could seriously interfere with the blood supply to the kidney.[13]

The temporary depression of arterial blood pressure observed in hypertensive dogs after renal decapsulation may be attributed to the rapid and extensive development of a collateral blood supply to the kidney. The gradual return to the previous pressure level suggests that, as the scar tissue capsule forms, it destroys a portion of the newly developed collateral supply. It is almost fifty years since Har-

rison[14] advocated renal decapsulation in order to increase the blood supply to the kidneys in Bright's disease. This procedure has since been used sporadically for many renal disorders and the reports are in disagreement as to its value. Our results indicate that when "improvement" occurred, it was of a temporary nature.

Several investigators are at present engaged in the attempt to produce an increased blood supply to the kidneys by various means. Cerqua and Samaan[2] have reported the cure of experimental renal hypertension by renal decapsulation and the establishment of intimate contact between the denuded areas and the spleen and the omentum. These workers showed that within a few days the blood pressure had returned to normal levels. Inspection of the kidney at this time showed well-developed blood vessels traversing the area between the decapsulated kidney and the omentum. At this time, surgical destruction of the collaterals resulted in a return to the hypertensive levels. This picture is similar to that which we have found, except that in our experiments the destruction of the collateral supply came about spontaneously with the growth and development of the scar tissue capsule.

Davis and Tullis[3] have recently reported their observations on the development of a large collateral blood supply by splitting the kidney and sewing in a portion of the omentum. MacNider and Donnelly[4] introduced omentum into a cortical slit and found that a considerable area of renal tissue received blood from this adventitious source. Mansfield, Weeks, Steiner, and Victor[5] reported that omentum-kidney pexis resulted in a temporary fall in the blood pressure of hypertensive dogs. However, spleen-kidney pexis was followed by a continuous decline to normal pressure lasting up to six months. Langeron and Camelot[15] have reported that renal decapsulation in five clinical cases of grave hypertension resulted in a transient fall in blood pressure lasting for only a few days, the blood pressure then returning to the previous level. Abrami, Isélin and Robert-Wallich[16] performed unilateral decapsulation and brought omental tissue into close contact with the denuded kidney in two clinical cases of renal hypertension but found no change in blood pressure. Bruger and Carter[17] have utilized a similar procedure. De Takats[18] found no improvement after such an operation. Thus, decapsulation with or without the production of a muscle bed or omental graft results in only an evanescent fall in blood pressure and fails to correct renal hypertension. The spleen-kidney pexis may offer better possibilities, but further investigation on this point is essential.

It should be kept in mind that the Goldblatt dog provides an animal on which the search for a method of alleviation of clinical hypertension is limited to that form which is due to partial occlusion of the main renal arteries. However, in the great majority of cases in man,

the symptom of hypertension is associated with partial occlusion of the renal arterioles rather than of the main renal arteries. Thus, an accessory blood supply to the kidney which might relieve the Goldblatt type of hypertension would not necessarily relieve hypertension in man. However, since the method which we describe does not alleviate even the Goldblatt type, its use on man is obviously unjustified as yet.

SUMMARY

Decapsulation and the production of a muscle bed for the ischemic kidneys in hypertensive dogs leads to a temporary fall in blood pressure, followed by a return to the hypertensive level within a few days. In normal dogs the procedure does not prevent the development of hypertension if the renal arteries are subsequently partially occluded.

There appears to be no evidence warranting the use of this procedure for the relief of hypertension in man.

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